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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,474	01/05/2006	Erik Rytter Ottosen	3893-0220PUS2	1370
2292 7590 02/09/2010 BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747				
EXAMINER KOSACK, JOSEPH R				
ART UNIT 1626		PAPER NUMBER		
NOTIFICATION DATE 02/09/2010		DELIVERY MODE ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

# Office Action Summary

## Application No.

10/563,474

## Applicant(s)

OTTOSEN ET AL.

## Examiner

Joseph R. Kosack

## Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 09 November 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 49, 50, 63-71, 77-81, 83, 88, 89, 91 and 92 is/are pending in the application.
- 4a) Of the above claim(s) 83, 88, 89 and 92 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 49, 50, 63-71, 77-81 and 91 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Claims 49, 50, 63-71, 77-81, 83, 88, 89, 91, and 92 are pending in the instant application.

#### ***Amendments***

The amendment filed on November 9, 2009 has been acknowledged and has been entered into the instant application file.

#### ***Previous Claim Rejections - 35 USC § 112***

Claims 49, 50, 63-71, 77-81 and 91 were previously rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for solvates in the solid form.

The Applicant has deleted the non-enabled subject matter, and the rejection is withdrawn.

#### ***Previous Claim Rejections - 35 USC § 103***

Claims 49, 63-65, 67, 69-71, 77, 78, 81, and 91 were previously rejected under 35 U.S.C. 103(a) as being unpatentable over Ottosen et al. (WO 2001/05744) in view of Revesz (WO 2002/76447).

The Applicant has traversed the rejection on the grounds that the references were combined by hindsight reconstruction, that the modifications are unpredictable, and that the instantly claimed compounds have better activity for IL-1B and TNF- $\alpha$  inhibition.

The Examiner respectfully disagrees.

Both Ottosen et al. and Revesz deal with TNF- $\alpha$  inhibitors. Ottosen et al. teach the template for the tricyclic core, the R2 substitution, the placement of the R3 and R4

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groups, and the other requirements for the compounds that are in the claims. Revesz teaches compounds that have the same tricyclic core, have fluorine for the R3 and R4 groups in the appropriate position, and all the other substituents other than the R2 groups.

Therefore, the person of ordinary skill in the art would be specifically motivated to combine the teachings of Ottosen et al. and Revesz in order to generate another compound that is capable of inhibiting IL-1B and TNF-a with a reasonable expectation of success since the compounds already have been shown to have that utility. Even though the Applicant has shown that the instantly claimed compounds have improved activity as IL-1B and TNF-a inhibitors, the Examiner does not believe that the results are strong enough to overturn the strong *prima facie* case of obviousness that has been set forth.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Therefore, the Applicant's arguments have been considered, but were not found to be persuasive. The rejection is maintained.

***Previous Double Patenting Rejections***

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Claims 49, 50, 63-71, 77-81 and 91 were previously rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,541,670 in view of Revesz (WO 2002/76447).

The Applicant has traversed the rejection on the grounds that the rejection is improper because the rejection is not based on a granted U.S. patent.

The rejection is over U.S. Patent No. 6,541,670, which is a granted U.S. patent with an inventor in common with the instant application. Therefore, the rejection is proper.

The rejection is maintained.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

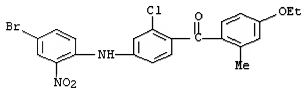
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were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 49, 63-65, 67, 69-71, 77, 78, 81, and 91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ottosen et al. (WO 2001/05744) in view of Revesz (WO 2002/76447)

Determination of the scope and content of the prior art (MPEP §2141.01)

Ottosen et al. teaches a compound of the formula



which corresponds to Formula I where R1

is methyl, R2 is chloro, there are two R3s and they are nitro and bromo, R4 is hydrogen, R5 is hydrogen, R6 is Y2-R9, Y2 is O, R9 is methyl substituted by 1 R7, and R7 is methyl. See Example 9, page 23.

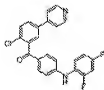
Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Ottosen et al. does not teach where R3 and R4 is fluorine where R3 is meta to R4 and para to the NH group.

Finding of prima facie obviousness—rational and motivation (MPEP §2142-2413)

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Revesz teaches various TNF alpha and IL1 beta inhibitors that have the desired three phenyl ring structure and the motif of the R3 and R4 groups such as



. See Example 3, page 14.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to synthesize the compound of Ottosen et al. and modify the R3 and R4 groups with the fluorine atoms of Revesz with a reasonable expectation of success. The motivation to make the claimed invention from the teachings of the prior art is provided by Revesz as Revesz teaches that the 2,4-difluorophenyl group is the especially preferred embodiment. See page 3, lines 13-14.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

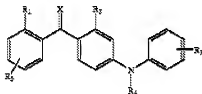
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 49, 50, 63-71, 77-81 and 91 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,541,670 in view of Revesz (WO 2002/76447). Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to the same art specific subject matter.

Determination of the scope and content of the prior art (MPEP §2141.01)

'670 teaches a genus of compounds of the formula



which overlaps with the instant claims where R4 is hydrogen, 1 or more R3 groups are fluorine with one at the 2-position, R5 can be amide, and all other substituents are as defined.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

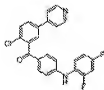
'670 does not teach specifically in the claims where R3 and R4 is fluorine where R3 is meta to R4 and para to the NH group.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)



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Revesz teaches various TNF alpha and IL1 beta inhibitors that have the desired three phenyl ring structure and the motif of the R3 and R4 groups such as



. See Example 3, page 14.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to synthesize the compound of '670 and modify the R3 and R4 groups with the fluorine atoms of Revesz with a reasonable expectation of success. The motivation to make the claimed invention from the teachings of the prior art is provided by Revesz as Revesz teaches that the 2,4-difluorophenyl group is the especially preferred embodiment. See page 3, lines 13-14.

### ***Conclusion***

Claims 49, 50, 63-71, 77-81 and 91 are rejected.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph R. Kosack whose telephone number is (571)272-5575. The examiner can normally be reached on M-Th 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Joseph R Kosack/  
Examiner, Art Unit 1626